Altered Fractionation in Radiation Therapy for Head and Neck Cancer

RADIATION THERAPY, alone or in combination with other treatment methods (such as surgical therapy), has been a standard treatment of cancer of the head and neck. A "conventional" course of curative radiation therapy has typically been a single daily dose of 180 to 200 cGy five days a week to a total of 6,600 to 7,200 cGy in 33 to 40 fractions over 6½ to 8 weeks. It has also been "hypofractionated" into as few as 1 to 24 fractions (usually ≥250 cGy) one to four times a week or "hyperfractionated" into as many as 40 to 80 fractions, giving multiple fractions in one day. Because hypofractionated regimens with curative intent have been fraught with both poor control rates and formidable complications, they are not generally recommended. Therefore, the rest of this discussion will concern hyperfractionation.

Two important radiobiologic principles support the use of hyperfractionated radiation therapy. First, the occurrence of long-term side effects—severe soft tissue fibrosis or necrosis—depends more on the size of each individual fraction than on the final total dose. A fraction size of 450 cGy can cause much more long-term damage than a fraction size of 180 cGy, even when the former is used in a course of treatment to the same or lower total dose. In addition, substantial biologic and clinical evidence shows that these fractions should be separated by approximate six-hour intervals to allow for sufficient repair of the long-term effects. Therefore, the total dose can be escalated higher than the conventional 6,600 to 7,200 cGy by treating with a smaller fraction size (less than 180 cGy). This is accomplished by treating twice a day to totals as high as 8,160 cGy. Acute mucosal or skin reactions remain unchanged, however, and actually may be more severe than with conventional radiotherapy.

Hyperfractionated regimens may be accelerated so that a total dose is completed in a shorter period than conventional radiotherapy. For instance, a regimen of 6,600 cGy may be completed in 5 weeks rather than 6½ to 8 weeks. This accelerated therapy counteracts tumor repopulation that can be an important factor in local failure. Just as in pure hyperfractionation (without being accelerated), long-term side effects are reduced, although acute mucosal or skin reactions are increased. Nearly all hyperfractionated regimens have incorporated some degree of acceleration. This can range from 110 to 160 cGy per fraction given twice a day to a total dose of 6,720 to 8,160 cGy over 6 to 7 weeks to 140 to 150 cGy per fraction given three times a day to a total of 5,040 to 5,400 cGy in 12 days. Three prospectively randomized studies have used hyperfractionation and have shown considerably improved local or regional control and complete response rates. One study has also shown notably improved disease-free and overall survival rates for the hyperfractionated group, and a second also showed a trend in survival improvement. Results of altered fractionation (hyperfractionation or accelerated hyperfractionation) have been promising and have gained acceptance, especially in the treatment of moderately advanced to advanced head and neck cancer.

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Captopril Renography for the Detection of Renovascular Hypertension

RENOVASCULAR DISEASE is an uncommon but important cause of hypertension. It is important because correcting the underlying disease can result in permanent cure and help preserve renal function. The prevalence of renovascular hypertension depends on several clinical risk factors. In patients with mild hypertension, the prevalence is probably less than 0.5%. It increases to about 5% to 15% in patients with severe hypertension, especially if the hypertension is refractory to standard therapy, the patients are young, are smokers, have an abrupt onset of hypertension, have an abdominal bruit, or have other evidence of vascular disease. In such patients a noninvasive test with good sensitivity and specificity has the highest clinical likelihood of ruling in or ruling out renovascular disease.

Until recently an isotope renogram using radioiodinated iodohippurate sodium (Hippuran) or technetium Tc 99m-labeled diethylenetriaminepentaacetic acid (DTPA, or technetium Tc 99m pentetate) was the screening test, but moderate specificity led to a substantial number of false-positive results. Thus, if the prevalence of disease is about 10% and the specificity is 70%, the positive predictive value of an abnormal test is only 25%. The introduction of captopril renography has increased both the sensitivity and specificity of the test, making it an almost ideal noninvasive screening test. The test involves an oral dose of a short-acting angiotensin-converting enzyme (ACE) inhibitor, usually captopril, in a dose of 25 to 50 mg. This medication causes a fall in glomerular filtration in the kidney supplied by an artery with a functionally notable stenosis. Either ^{99m}Tc pentetate or ^{99m}Tc mertiatide (mercaptoacetyltriglycine) can be used as the radiopharmaceutical agent. The uptake of the radiopharmaceutical in an abnormal kidney is slower and the maximum uptake in that kidney is seen later than in normal kidneys. One approach is to complete a captopril renogram first and, if it is normal—that is, there is no asymmetry in perfusion and excretion between the kidneys—no additional testing is required. Renovascular hypertension is excluded with a high degree of confidence (90% to 95%). When there is asymmetry with reduced glomerular filtration and an increased transit time on one side, we repeat the study with

the patient off ACE inhibitors. If the second study shows a return to normal, that strongly suggests that a functional stenosis is present. We advise patients to stop taking diuretics before the test, but not all investigators agree that this increases the diagnostic value.

Several series are comparing this functional imaging study with the gold standard, which is the correction of hypertension when the stenotic lesion is treated either by angioplasty or surgical repair. Based on several studies, sensitivity and specificity are both around 90% to 95%. It is noteworthy that renal arteriogram is not considered the gold standard because there can be stenotic lesions that are not functionally important. Nevertheless, contrast arteriography is an essential part of evaluation in those patients who have an abnormal captopril renogram and who are candidates for surgical correction.

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Managing Hickman Catheter Problems Without Surgery

HICKMAN CATHETERS are commonly used for long-term central venous access. These catheters are usually inserted through the subclavian vein and then tunneled for stability and to prevent infection. As with any central venous line, complications are encountered in both placing and maintaining the patency of this catheter. These complications include catheter malposition, intraluminal thrombosis, and occlusion of the catheter tip by a fibrin sheath. These problems can often be managed with nonoperative, fluoroscopically guided manipulations.

The most common problem after a Hickman catheter is successfully inserted is malposition of the catheter tip. This occurs most frequently into the ipsilateral internal jugular vein. Extension from the right subclavian vein into the left subclavian through the brachiocephalic vein may also be observed. Repositioning the catheter tip into the superior vena cava is generally not difficult. This is accomplished by inserting a catheter into the femoral vein. This catheter is guided fluoroscopically into the upper thorax through the venous system. The catheter tip is positioned cephalic to the Hickman line and then deflected caudally with a tip-deflecting wire. In most cases, the Hickman line will be pulled into proper position as the angiographic catheter is pulled away.

To avoid problems with catheter malposition, many physicians prefer that central venous lines be placed by an interventional radiology team, where suitable fluoroscopic imaging and catheter-inserting skills are readily available. Moreover, ultrasonographic guidance may be used to direct the venous puncture, reducing the chance of inadvertent subclavian arterial puncture, which can be associated with bleeding complications. In addition, if a complicating pneumothorax develops, it can be recognized and evacuated immediately without awaiting a postprocedural chest x-ray film.

Thrombosis of the central line may also be managed successfully in most cases. Instilling 50,000 to 100,000 units of urokinase will frequently lyse the occluding thrombus. If this is unsuccessful, directing an angiographic guide wire under fluoroscopic observation will often dislodge the thrombus.

An encasing fibrin sheath at the catheter tip causing line occlusion is a more difficult problem to manage. Two techniques have been used to approach this problem. The first involves placing a wire with a tight J tip through the catheter, stripping the fibrin from the tip. The second method is to insert a femoral venous catheter and manipulate an encircling snare around the Hickman catheter. As the snare is pulled caudally, the fibrin sheath is peeled away from the central venous line. Using this method, a 95% success rate in restoring patency and function has been reported.

Interventional radiologic techniques are effective in preserving the long-term patency of Hickman catheters and obviate the need for surgical replacement in most patients.

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Three-Dimensional Spiral Computed Tomographic Angiography

THREE-DIMENSIONAL SPIRAL computed tomographic (CT) angiography is a new technique for obtaining images of the vascular system noninvasively. Unlike conventional CT scanners, spiral computed tomography combines continuous tube rotation with a continuous table feed. This allows a region of the body to be studied during a single breath-hold, thus eliminating most motion and respiratory artifacts. A volumetric data set can be acquired that can be timed with an intravenous bolus during either the arterial or venous phase of the injection for abdominal studies. The arterial phase starts about 15 to 20 seconds after the start of the intravenous injection. Once the data set is acquired, it is edited to obtain three-dimensional images of the vascular system. Editing eliminates overlying soft tissues and bony structures, producing a "subtraction angiogram" with either a shaded surface display or maximal intensity projection format.

To date, the most common clinical indications for three-dimensional spiral CT angiography include evaluation of the abdominal aorta and its branches, the pul-